Complete Summary

GUIDELINE TITLE

National Academy of Clinical Biochemistry laboratory medicine practice guidelines: Use of cardiac troponin and B-type natriuretic peptide or N-terminal proB-type Natriuretic Peptide for Etiologies other than acute coronary syndromes and heart failure.

BIBLIOGRAPHIC SOURCE(S)

Wu AH, Jaffe AS, Apple FS, Jesse RL, Francis GL, Morrow DA, Newby LK, Ravkilde J, Tang WH, Christenson RH, Cannon CP. National Academy of Clinical Biochemistry laboratory medicine practice guidelines: use of cardiac troponin and B-type natriuretic peptide or N-terminal proB-type natriuretic peptide for etiologies other than acute coronary syndromes and heart failure. Clin Chem 2007 Dec 1;53(12):2086-96. [109 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Wu AH, Apple FS, Gibler WB, Jesse RL, Warshaw MM, Valdes R Jr. National Academy of Clinical Biochemistry Standards of Laboratory Practice: recommendations for the use of cardiac markers in coronary artery diseases. Clin Chem 1999 Jul;45(7):1104-21. [119 references] PubMed

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s)/intervention(s) for which important revised regulatory and/or warning information has been released.

- June 8, 2007, Troponin-I Immunoassay: Class I Recall of all lots of the Architect Stat Troponin-I Immunoassay. The assay may report falsely elevated or falsely decreased results at and near a low level, which may impact patient treatment.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Chronic renal failure
- Other non-ischemic etiologies, such as:
  - Blunt chest trauma
  - Critical illness
  - Congestive heart failure
  - Pulmonary embolism
  - Sepsis
  - Myocarditis
- Cancer being treated with cardiotoxic chemotherapies
- Conditions and diseases requiring non-cardiac surgery, such as vascular surgery
- Conditions and diseases requiring percutaneous coronary intervention (PCI)
- Conditions and diseases requiring cardiac surgery
- Conditions or diseases without overt ischemic heart disease where cardiac troponins may be elevated (refer to Table 6-1 in the original guideline document)
- Conditions or diseases without overt heart failure where concentrations of B-type natriuretic peptide/N-terminal B-type natriuretic peptide (BNP/NT-proBNP) may be increased (refer to Table 6-2 in the original guideline document)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Risk Assessment

CLINICAL SPECIALTY

Cardiology
Critical Care
Emergency Medicine
Family Practice
Internal Medicine
Nephrology
Oncology
Pathology
Pulmonary Medicine

Surgery
Thoracic Surgery

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Clinical Laboratory Personnel
Emergency Medical Technicians/Paramedics
Health Care Providers
Hospitals
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To present recommendations on the interpretation of cardiac troponins (cTn) and the natriuretic peptides in etiologies other than acute coronary syndromes and heart failure

TARGET POPULATION

Patients with conditions or diseases other than acute coronary syndrome and heart failure that may affect changes in cardiac biomarkers

INTERVENTIONS AND PRACTICES CONSIDERED

Use of cardiac troponin (cTn) and B-type natriuretic peptide (BNP) or N-terminal proB-type natriuretic peptide (NT-proBNP) in specific settings (e.g., evaluation of chronic renal failure, non-ischemic etiologies, post-surgery and post percutaneous coronary intervention [PCI])

MAJOR OUTCOMES CONSIDERED

Usefulness/efficacy of cardiac biomarker utilization in specific settings for diagnosis and/or risk assessment of morbidity, mortality, and adverse cardiac events

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

These National Academy of Clinical Biochemistry (NACB) guidelines were developed rigorously; however it was possible to include only papers published in the English language. The specified method for developing the evidence base for recommendations listed involved use of PubMed, EMBASE, and other databases that were not necessarily published. Systematic methods were used whenever available; searches were first set to be sensitive to avoid missing papers of possible interest, and then narrowed to sort through the literature in order to enhance specificity. The writing group contacted recognized experts to assure that important evidence had not been missed.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Weight of Evidence

A - Data derived from multiple randomized or appropriately designed clinical trials that involved large numbers of patients

B - Data derived from a limited number of randomized or appropriately designed trials that involved small numbers of patients or from careful analyses of observational registries

C - Expert Consensus was the primary basis for the recommendation

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The National Academy of Clinical Biochemistry's (NACB) Laboratory Medicine Practice Guidelines (LMPG) for use of cardiac markers in coronary artery diseases were published in July of 1999. Since production of this initial document,

numerous published studies and presented data have added significantly to the knowledge base for cardiac biomarkers. This increased knowledge has substantially expanded the scope of recommendations for cardiac biomarker utilization since the 1999 document, and in particular has required the inclusion of recommendations regarding biomarkers that extend beyond myocardial necrosis. Toward addressing these advances and their impact on biomarker utilization in clinical practice, the NACB appointed a chair and members of a LMPG committee that was charged with the overall objective of revising and extending the earlier recommendations by establishing modern guidelines for Utilization of Biomarkers in Acute Coronary Syndrome and Heart Failure. This LMPG is aimed at providing analytical and clinical guidance for the measurement and interpretation of cardiac biochemical markers of acute coronary syndromes (ACS), heart failure and point-of-care measurement and logistics of providing ACS biomarker data for patient care; guidance for interpretation of biomarkers in etiologies other than ACS and Heart Failure is included as well.

These guidelines and their recommendations are structured into six chapters that include Chapter 1: Clinical Utilization of Biomarkers in Acute Coronary Syndromes (ACS); Chapter 2: Analytical Issues of ACS Biomarkers; Chapter 3: Clinical Utilization of Biomarkers of Heart Failure; Chapter 4: Analytical Issues of Heart Failure Biomarkers; Chapter 5: Point of Care Testing and Logistics; and Chapter 6: Cardiac Biomarkers and Other Etiologies. Each chapter was spearheaded by a writing group, which was a subset of the overall committee. In addition, other ad hoc expertise contributed to the writing group of some subsections and chapters to optimize the content and quality of the guidelines. The "questions" for each chapter are in the form of issues addressed and specified in the organization of each individual chapter. The chapter design of the guidelines was used to facilitate finding guidance by users; this format was also used, in part, to provide an easy and focused procedure for updating the guidelines in the future. Also, the chapter design allowed publication of sections in appropriate laboratory medicine and clinical specialty journals.

Stakeholder involvement in development and refinement of these guidelines was substantial. The guideline team was comprised of laboratory medicine, ACS cardiology experts, and heart failure cardiology experts. As these guidelines target acutely ill patients, Emergency Medicine stakeholders were represented by a specialist; it is also noteworthy that all of the laboratory professionals and cardiology experts on the guideline committee have substantial interaction, knowledge, and publications in the area of laboratory and clinical medicine in the Emergency Medicine environment.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Modified American College of Cardiology/American Heart Association Classifications: Summary of Indications

Class I: Conditions for which there is evidence and/or general agreement that a given laboratory procedure or treatment is useful and effective.

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a laboratory procedure or treatment.

Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.

Class IIb: Usefulness/efficacy is less well established by evidence/opinion.

Class III: Conditions for which there is evidence and/or general agreement that the laboratory procedure/treatment is not useful/effective and in some cases may be harmful.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Stakeholder involvement in development and refinement of these guidelines was substantial. To further enhance stakeholder input, draft revisions of the Guidelines were prepared and placed for comment on the National Academy of Clinical Biochemistry (NACB) World Wide Web site (http://www.aacc.org/AACC/members/nacb/LMPG/OnlineGuide/DraftGuidelines/BioHearFailure/). The draft Laboratory Medicine Practice Guidelines (LMPG) and suggested revisions were also presented for public and stakeholder comment at the October 2004 Arnold O. Beckman Conference titled *Cardiac Markers: Establishing Guidelines and Improving Results*. Refer to Table 1 of the Preamble to the original guideline document for a list of the various stakeholder groups that agreed to examine the documents and were represented at the conference.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions of the weight of evidence (A-C) and the summary of indications (Classes I, II, IIa, IIb, III) are presented at the end of the "Major Recommendations" field.

Note from the National Academy of Clinical Biochemistry (NACB) and the National Guideline Clearinghouse (NGC)*: The Laboratory Medicine Practice Guidelines (LMPG) for utilization of biochemical markers in acute coronary syndromes and heart failure* have been divided into individual summaries. In addition to the current summary, the following are available:

- Chapter 1: Clinical characteristics and utilization of biochemical markers in acute coronary syndromes
- Chapter 2: Analytical issues for biochemical markers of acute coronary syndromes

- Chapter 3: Clinical utilization of cardiac biomarker testing in heart failure
- Chapter 4: Analytical issues for biomarkers of heart failure
- Chapter 5: Point of care testing, oversight and administration of cardiac biomarkers for acute coronary syndromes

Use of Cardiac Biomarkers in the Evaluation of Patients with Chronic Renal Failure

Utilization of Cardiac Biochemical Marker in the Setting of Chronic Renal Failure

Recommendations for use of biochemical markers in the setting of chronic renal failure

Class I

1. In renal failure patients with symptoms (e.g., acute chest pain), electrocardiographic (ECG) or other clinical evidence suggesting myocardial ischemia, measurement of cardiac troponin (cTn) is warranted for evaluation of myocardial infarction (MI). **(Level of Evidence A)**
2. For end-stage renal disease (ESRD) patients, as for all patients who may have baseline elevations of cTn, who present with possible acute coronary syndrome (ACS), relying on dynamic changes in the cTn values of 20% or more should be used to define those with acute myocardial infarction. **(Level of Evidence B)**

Class IIb

1. cTnT and cTnI can be used as aids for defining the risk for mortality in ESRD patients and to provide baseline values for comparison when measured in the setting of an acute clinical change. **(Level of Evidence B)**
2. In renal failure patients, B-type natriuretic peptide (BNP) or N-terminal B-type natriuretic peptide (NT-proBNP) testing can be used in the acute setting to *rule out* or to *confirm* the diagnosis of heart failure among patients presenting with ambiguous signs and symptoms. However different decision point (cutoff) values must be used compared to patients with estimated glomerular filtration rate >60 mL/min/1.73m^2. **(Level of Evidence B)**

Class III

1. Routine BNP/NT-proBNP measurement is not warranted in asymptomatic end-stage renal disease patients. **(Level of Evidence B)**

Use of Biomarkers in the Evaluation of Other Non-Ischemic Etiologies

Use of Cardiac Biomarkers in the Setting Non-ischemic Etiologies

Recommendations for use of biochemical markers in other non-ischemic etiologies

Class IIb

1. Increased cardiac telemetry may be warranted for patients who have increased cTn values following blunt chest trauma. **(Level of Evidence B)**
2. The measurement of cTn can be used to define risk among patients who are critically ill. **(Level of Evidence A)**
3. Increased cTn values identify individuals at increased risk for the development of congestive heart failure when treated with adriamycin therapy for cancer. **(Level of Evidence B)**
4. Increased cTn values identify individuals at increased risk with acute pulmonary embolism. **(Level of Evidence B)**
5. Routine BNP/NT-proBNP measurements may be warranted among patients with non-ischemic etiologies such as sepsis, myocarditis, or pulmonary embolism. **(Level of Evidence C)**

Class III

1. Release of cTn from patients with cancer undergoing cardiotoxic chemotherapies represents myocardial damage, which may be associated with a worse prognosis **(Level of Evidence B)**. However routine cTnT or cTnI measurements are not warranted among cancer patients undergoing chemotherapies that are toxic to the heart (except those receiving adriamycin). **(Level of Evidence C)**

Use of Biomarkers after Non-cardiac Surgery

Use of Cardiac Biochemical Markers After Non-cardiac Surgery

Recommendations for use of cardiac markers after non-cardiac surgery

Class IIb

1. cTnT and cTnI are recommended for patients undergoing non-cardiac surgery if there is a question of cardiac ischemia. Cutoff concentrations that are used for diagnosis of MI are appropriate. **(Level of Evidence C)**
2. cTnT and cTnI are recommended for post-surgical assessment of patients undergoing vascular surgery given the high frequency of underlying coronary artery disease and associated perioperative events. Such increases appear to be due to ischemia and are highly prognostic for both short- and long-term mortality. Cutoff concentrations that are used for diagnosis of MI are appropriate. **(Level of Evidence B)**
3. Increases of cTn post operatively are associated with adverse prognosis and should prompt clinical follow up. **(Level of Evidence B)**

Class III

1. Routine BNP/NT-proBNP measurements are not warranted among patients undergoing non-cardiac surgery. **(Level of Evidence C)**

Biomarker Use after Percutaneous Coronary Intervention (PCI)

Use of Cardiac Biochemical Markers after PCI

Recommendations for use of biomarkers after PCI

Class IIb

1. It is appropriate to measure cTnT or cTnI before and after percutaneous coronary intervention to determine the presence of ischemic cardiac damage if the baseline pre-procedural value is less than 99th percentile for the reference control population. Any increase is indicative of cardiac damage. However, there is currently insufficient evidence to recommend the specific cTn cutoff concentration. **(Level of Evidence C)**

Class III

1. Routine BNP/NT-proBNP measurements are not warranted among patients undergoing PCI. **(Level of Evidence C)**
2. If the pre-procedural baseline cTn is increased above the 99th percentile of a reference control population, then biochemical markers should not be used to estimate whether increases are related to the procedure or to progression of the underlying disease state that caused the need for the procedure. If serial preprocedural cTn values are available, a falling trend followed by a post-procedural increase of 20% or more may be indicative of new myocardial injury, even if any or all of the pre-procedural results are above the 99th percentile. **(Level of Evidence C)**

Use of Biomarkers after Cardiac Surgery

Use of Cardiac Biochemical Markers after Cardiac Surgery

Recommendations for use of biomarkers after cardiac surgery

Class IIa

1. The higher the cTn values post operatively, the greater the risk of adverse cardiac events. **(Level of Evidence B)**
2. In addition to greater than 5-fold increase in cTn after the procedure, clinical and other (non-lab medicine) diagnostic testing criteria should be used to distinguish components related to the operative procedure and cardioprotection from vascular events. **(Level of Evidence C)**
3. Preprocedural baseline cTn increases help to define risk among patients undergoing cardiac surgery. **(Level of Evidence C)**

Class III

1. At this time, there is insufficient evidence to recommend routine measurement of BNP/NT-proBNP before or after cardiac surgery. **(Level of Evidence C)**

Definitions:

Weight of Evidence

A - Data derived from multiple randomized or appropriately designed clinical trials that involved large numbers of patients

B - Data derived from a limited number of randomized or appropriately designed trials that involved small numbers of patients or from careful analyses of observational registries

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Summary of Indications

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>
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CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate utilization of biochemical markers for evaluation and risk stratification in settings other than acute coronary syndromes (ACS) and heart failure (HF)

POTENTIAL HARMS

False positive increases in cardiac troponin (cTn), B-type natriuretic peptide (BNP) and N-terminal B-type natriuretic peptide (NT-proBNP) can occur, although very infrequently, as a result of analytical errors. Although the incidence of assay

interferences caused by atypical antibodies has been reduced, all immunoassays have the potential for both false positive and false negative interferences.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The materials in this publication represent the opinions of the authors and committee members, and do not represent the official position of the National Academy of Clinical Biochemistry (NACB). The National Academy of Clinical Biochemistry is the academy of the American Association for Clinical Chemistry.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Wu AH, Jaffe AS, Apple FS, Jesse RL, Francis GL, Morrow DA, Newby LK, Ravkilde J, Tang WH, Christenson RH, Cannon CP. National Academy of Clinical Biochemistry laboratory medicine practice guidelines: use of cardiac troponin and B-type natriuretic peptide or N-terminal proB-type natriuretic peptide for etiologies other than acute coronary syndromes and heart failure. Clin Chem 2007 Dec 1;53(12):2086-96. [109 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 Jul (revised 2007 Dec)

GUIDELINE DEVELOPER(S)

National Academy of Clinical Biochemistry - Professional Association

SOURCE(S) OF FUNDING

National Academy of Clinical Biochemistry

GUIDELINE COMMITTEE

The National Academy of Clinical Biochemistry

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

National Academy of Clinical Biochemistry (NACB) Writing Group Members: Alan B. Storrow, MD, Section Leader; Fred S. Apple, PhD; Alan H.B. Wu, PhD; Robert L. Jesse, MD, PhD; Gary S. Francis, MD; Robert H. Christenson, PhD

NACB Committee Members: Robert H. Christenson, *Chair*, University of Maryland School of Medicine, Baltimore, Maryland, USA; Fred S. Apple, Hennepin County Medical Center and University of Minnesota, Minneapolis, Minnesota, USA; Christopher P. Cannon, Brigham and Women's Hospital, Boston, Massachusetts, USA; Gary S. Francis, Cleveland Clinic Foundation, Cleveland, Ohio, USA; Robert L. Jesse, Medical College of Virginia, Richmond, Virginia, USA; David A. Morrow, Brigham and Women's Hospital, Boston, Massachusetts, USA; L. Kristin Newby, Duke University Medical Center, Durham, North Carolina, USA; Jan Ravkilde, Aarhus University Hospital, Aarhus, Denmark; Alan B. Storrow, Vanderbilt University, Nashville, Tennessee, USA; W. H. Wilson Tang, Cleveland Clinic Foundation, Cleveland, Ohio, USA; Alan H. B. Wu, San Francisco General Hospital and University of California at San Francisco, San Francisco, California, USA

Ad Hoc members of the committee for selected sections: Allan S. Jaffe, Mayo Clinic, Rochester, Minnesota, USA; Alan S. Maisel, University of California at San Diego, San Diego, California, USA; Mauro Panteghini, University of Milan, Milan, Italy

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Other than modest funding from the National Academy of Clinical Biochemistry/American Association for Clinical Chemistry (NACB/AACC), development of these guidelines was a volunteer activity. Thus the guidelines are editorially independent from any funding body.

All potential conflicts of interest for the NACB guidelines committee and ad hoc members of the writing committees are listed at the following: http://www.aacc.org/AACC/members/nacb/LMPG/OnlineGuide/PublishedGuidelines/ACSHeart/heartpdf.htm.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Wu AH, Apple FS, Gibler WB, Jesse RL, Warshaw MM, Valdes R Jr. National Academy of Clinical Biochemistry Standards of Laboratory Practice: recommendations for the use of cardiac markers in coronary artery diseases. Clin Chem 1999 Jul;45(7):1104-21. [119 references] PubMed

GUIDELINE AVAILABILITY

Electronic copies: Available from the National Academy of Clinical Biochemistry (NACB) Web site.

Print copies: National Academy of Clinical Biochemistry publications are available through American Association for Clinical Chemistry (AACC) Press. To make a purchase or request a catalog, contact AACC Customer Service at 202-857-0717 or custserv@aacc.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Preamble. National Academy of Clinical Biochemistry laboratory medicine practice guidelines for utilization of biochemical markers in acute coronary syndromes and heart failure. Washington (DC): National Academy of Clinical Biochemistry (NACB); 2007. p. 1-3.

Electronic copies: Available from the National Academy of Clinical Biochemistry (NACB) Web site.

Print copies: National Academy of Clinical Biochemistry publications are available through American Association for Clinical Chemistry (AACC) Press. To make a purchase or request a catalog, contact AACC Customer Service at 202-857-0717 or custserv@aacc.org.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on March 12, 2008. The information was verified by the guideline developer on April 2, 2008.

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